COMMENTARY

Surface-adaptive interfaces: Bioresorbable ultrasound biomedical devices for noninvasive monitoring and imaging of deep-tissue homeostasis

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Homeostasis, a self-regulating process within our bodies, dynamically adjusts internal conditions to maintain equilibrium in response to external challenges. Monitoring homeostasis provides valuable pathophysiological insights for patients, particularly after surgery, while traditional clinical instruments that are capable of monitoring various physiological parameters such as body temperature, blood pressure, and blood glucose levels facilitate real-time health management for individuals and healthcare professionals.[1] Nevertheless, current medical approaches for regular deep-tissue homeostasis monitoring systems confront critical obstacles, notably in terms of their invasiveness, sensitivity, and ability for continuous monitoring, including[1] (1) insufficiency in multimodal sensing capability at shallow depths, (2) inadequate adaptation to the shapes and contours of tissues, and (3) sluggish responses to changes in the fluid dynamics and movements of organs or tissues. Specifically, technologies like X-ray imaging, computed tomography, and biopsies, for instance, are generally cumbersome, expensive, and impractical for ongoing and real-time monitoring. Additionally, for the aforementioned techniques, a lack of sensitivity for detecting early changes in tissue homeostasis or the aptitude for efficiently tracking patient health status post-surgery is generally observed.[2]

Soft bioelectronics, which can be seamlessly applied to human skin for biosensing, offer potential applications in portable monitoring of deep-tissue homeostasis, attributed to their softness, lightweight nature, and high sensitivity.[3] The development of flexible materials has contributed to the fabrication of soft bioelectronics as implantable devices with high surface adaptability, bioresorbability, and bioresponsibility, which ensures an improved precise and custom fit to the contours of the deep organ or tissue, enhancing the precision of the physiological detection and adhesion between the device and the biological surface.[4] Furthermore, the incorporation of imaging techniques, like ultrasound or photoacoustic technologies, into the soft substrates through

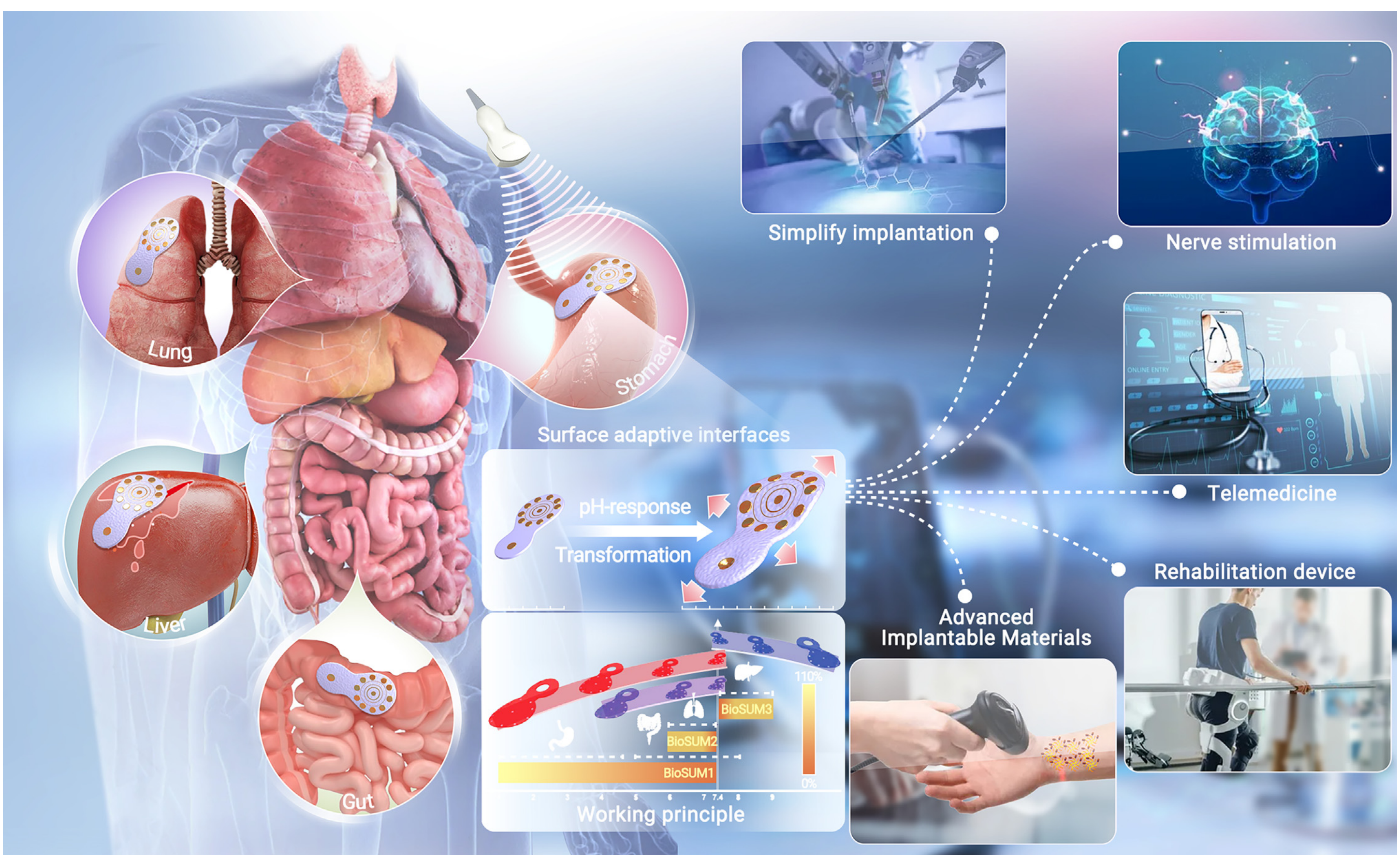

Figure 1. The concept of surface-adaptive interfaces for noninvasive imaging and monitoring of deep-tissue homeostasis Further efforts include advanced implantable materials, rehabilitation devices, telemedicine, nerve stimulation, simplified implantation, and other related improvements.

microfabrication technologies offers spatiotemporal information of applied surface through imaging instruments. Thus, the surface-adaptive bioelectronics integrated imaging system enabled the detection of homeostatic relative information such as pH, diameter, and temperature at the deep-tissue level.

Most recently, Liu et al.[5] in Prof. John Rogers' group proposed a bioresorbable shape-adaptive and bioresorbable materials structure (BioSUM) that enables continuous monitoring of deep-tissue homeostasis through the conventional ultrasound method. The BioSUM is composed of a soft and thin pH-responsive hydrogel matrix for swelling and a systematic array of bioresorbable metal disks for generating clear contrasts in ultrasound images due to their acoustic impedance mismatch with surrounding tissues. The thin and soft nature of the BioSUM exhibits strong flexibility and shape adaptivity, which can be twisted and wrapped around a tube and bent, respectively. Therefore, the BioSUM can be easily inserted through a trocar during laparoscopic surgery, attached to tissue via suturing, or affixed directly onto a targeted area with the use of an adhesive. The metal indicators are strategically positioned and selected to respond to environmental conditions within the body and alter the distribution between indicators based on local biochemical changes. The compositions of the BioSUM are bioresorbable, and therefore, the necessity of removing the device or any remnants of the interfaces can be omitted with high convenience.

In this article, the author skillfully utilizes pH-responsive hydrogels to sense changes in the pH values of the tissue microenvironment in the disease site inside the body. Liu et al. proposed three versions of BioSUM, which can be applied in three different situations: detection of pH range of leakage stomach, gut, and pancreas, respectively. Notably, the selection of bioresorbable metals and hydrogel materials, which dissolve and undergo hydrolytic chain scissions in biofluids, results in their transformation into harmless substances within well-defined timescales. The leakage of gastrointestinal fluids after gastroenterostomy might cause a significant shift in the local pH equilibrium, causing fluid to spread through the peritoneal cavity and, thus, organ damage. Such a change in pH would lead to a corresponding transformation in the state of the pH-responsive hydrogels. This transformation would further cause a change in the spatial relative positions of the metal arrays, which could ultimately be detected using conventional ultrasound devices. This capability is particularly useful for monitoring post-surgical recovery, including potential complications like leaks at surgical sites. Liu et al. systematically investigated the effect of the BioSUM on the gastrointestinal organs of rats and pigs for 14 days by creating a gastrointestinal leak surgically. As a result, the BioSUM could rapidly detect changes in the geometry of visual indicators (metal disc array) within 10 min in rats and 30 min in pigs, respectively. Ultrasound imaging data collected from commercial devices effectively reveal the existence and scale of leaks, demonstrating the potential application of the BioSUM in noninvasive monitoring and imaging of deep-tissue homeostasis after surgery. During the wound-closing stage, the surgeon can affix the biodegradable functional soft patch onto the affected area, thereby enabling the patient to monitor their health status at home by themselves.

In addition to the post-surgical monitoring, this kind of biodegradable functional soft patch further introduces a novel clinical strategy of noninvasive physiological signal detection within deep tissue-utilizes a multifunctional matrix embedded in an implantable interface or structure designed to interact directly with deep tissue multifunction of matrix of the implantable interface/structure to interactive with the deep tissue, thereby facilitating the transfer of detected signals to an imaging system for interpretation. The pH response hydrogel matrix of the BioSUM enables the device to observe changes in the surrounding pH levels. This transformation from a chemical to a physical signal could be detected by an imaging system, which then converts the physical signal into electrical signals for further analysis. Inspired by this design, a potential application of the biodegradable functional device is its interaction with a variety of physiological parameters beyond pH changes, including fluctuations in blood lipids, the presence of pathogens, and variations in hemoglobin levels. As a versatile biosensor, it has the potential to significantly reduce the need for repeated invasive procedures, such as blood draws, by monitoring the body's response to medications or detecting early signs of infection, especially in areas with limited medical resources.

Achieving practical applications requires both functionality and convenience. Addressing the numerous technological challenges and research opportunities ahead is essential (Figure 1). Initially, the current study of bio-responsive interfaces primarily focuses on single-component responses, such as sensitivity to pH, temperature, and humidity. This would enable a multitype response in various body fluid environments, including urine, saliva, and tears. Additionally, there is potential for extending this research to incorporate surface-adaptive materials in rehabilitation devices, such as braces and supports. By adapting to the patient's movement and body dynamics, these materials could significantly enhance patient comfort and improve the effectiveness of the rehabilitation process. This innovative approach to biosensing leverages spatiotemporal data to monitor changes in deep tissues after surgery, offering a distinctive and efficient method for evaluating patient recovery and tissue health post-operation. Moreover, the integration of soft interfaces with diverse imaging technologies, machine learning, and remote medicine could broaden their applicability in telemedicine, enhancing their utility across a wide range of remote medical services.

The adaptability and broad potential applications of biodegradable functional devices underscore the importance of further research into continuous, at-home health monitoring solutions. This exploration into noninvasive, continuous monitoring devices like the BioSUM could revolutionize patient care, particularly for those with chronic conditions or in post-operative recovery, by providing real-time health data without the need for frequent hospital visits. In addition to facilitating at-home health monitoring, the combination of the BioSUM and imaging technologies such as photoacoustic imaging and ultrasound imaging can provide a potential application for real-time monitoring of the implantable diagnostic devices inside tissue more directly, such as by tracking microrobots within tissues by leveraging photoacoustic imaging technology. Furthermore, photoacoustic imaging can also provide functional parameters in real time, allowing for important data to be collected for at-home monitoring from a multiscale perspective. Surface-adaptive-material-based microrobots can be seamlessly applied to the tissue surface, and the physical transformations of these microrobots can provide valuable insights into the condition and characteristics of the applied tissue surface.

In the realm of clinical applications, the proposed interfaces herald a promising future direction in medical technology. At its core, the surface-adaptive technology leverages a soft substrate that is highly versatile, going beyond mere structural support to incorporate features that are implantable, bioresorbable, and bioresponsive. This technology suggests a potential way to simplify the implantation procedure by using supercontraction to tightly conform around nerves, muscles, and hearts of various sizes when moistened. Finally, surface-adaptive materials are also suitable for rehabilitation devices, such as braces and supports, which could enhance patient comfort and improve the effectiveness of the rehabilitation process by adapting to the patient's movement and body dynamics. The future direction of the BioSUM encompasses the multifunctionality of the implantable soft patch, enabling it to respond to a variety of biological signals. Coupled with machine learning algorithms, these devices have high potential for diagnosing various homeostatic conditions based on data collected from the functional soft interface. As research and development continue to push the boundaries of possibility, the future of soft bioelectronics in transforming healthcare and enhancing patient outcomes appears exceedingly promising.

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DECLARATION OF INTERESTS

The authors declare no competing interests.